

IN THE CLAIMS:

Please amend claims 1, 2, 5-9, 11, 14-16, and 19-22 as follows. A marked-up copy of the claims is attached.

1. (Amended) A method for screening of the presence or absence of variation in a portion of a nucleic acid comprising the steps of:
- (a) preparing a test nucleic acid corresponding to the portion;
 - (b) preparing a full match probe having a base sequence fully complementary to a wild-type sequence of the portion, and a plurality of mismatch probes having a base sequence not complementary to the wild-type sequence;
 - (c) fixing the full match and mismatch probes separately to form a plurality of regions in accordance with a number of mismatches on a surface of a substrate to prepare a DNA array substrate;
 - (d) reacting the test nucleic acid with the probes on the DNA array substrate;
 - (e) measuring a signal intensity of each region as a total of signals originating from respective hybrids formed between the test nucleic acid and the probes to obtain a histogram pattern of signal intensity of the regions; and
 - (f) determining the presence or absence of mutation in the test nucleic acid comparing with the histogram pattern with a histogram pattern obtained using an array substrate obtained by the step (b) and a reference nucleic acid having the wild-type sequence.

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2. (Amended) The method according to claim 1, wherein the signal is a light and a total light quantity emitted from each region is measured as the signal intensity.

5. (Amended) The method according to claim 1, wherein the steps (c) to (f) further comprise:

(c) preparing separated regions on a substrate by fixing probes on a surface of the substrate, wherein the separate regions comprise:

a first region containing probes which provide a signal of a certain intensity on reaction with a nucleic acid having the wild-type sequence,

a second region containing probes which provide weaker signals on reaction with the reference nucleic acid, and

the third region containing probes which do not form hybrids on reaction with the reference nucleic acid;

(d) reacting the DNA array of the step (c) with the reference nucleic acid and measuring a signal of at least one region selected from the three regions to obtain a first pattern;

(e) reacting the DNA array of the step (c) with the test nucleic acid, and measuring a signal of at least one region selected in the step (d) to obtain a second pattern; and

(f) determining the presence or absence of variation in the test nucleic acid by comparing the first and second patterns.

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6. (Amended) The method according to claim 5, wherein the selected region is the first region giving a strongest total signal and/or the third region giving no or a weakest signal on reaction with the reference nucleic acid.

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7. (Amended) The method according to claim 5, wherein the separate regions are arranged on the substrate in order of signal intensity along a direction of a detection, wherein the signal intensity is obtainable on a reaction with the reference nucleic acid.

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8. (Amended) The method according to claim 5, wherein the selected region is the third region, and the test nucleic acid is determined to have variation when the signal is detected in the third region with the test nucleic acid in the step (e).

9. (Amended) The method according to claim 5, wherein the first region contains probes consisting of the full match probe and the mismatch probes having a one-base mismatch to the wild-type base sequence.

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11. (Amended) The method according to claim 5, wherein all three regions are selected and the presence of absence of variation is determined by comparing the histogram pattern of signal intensity.

14. (Amended) The method according to claim 1, wherein a base length of the probes is 8 to 30 nucleotides.

15. (Amended) The method according to claim 14, wherein the base length of the probes is 12 to 25 nucleotides.

16. (Amended) A DNA array substrate for screening a variation in a portion of a nucleic acid comprising:

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a full match probe fully complementary to a wild-type sequence of the portion, and a plurality of mismatch probes having at least one base mismatch to the wild-type sequence arranged on the substrate,

wherein the probes are arranged to form at least two separate regions selected from:

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a first region containing at least one probe which provides a signal of a certain intensity on reaction with a reference nucleic acid having the wild-type sequence,

a second region containing at least one probe which provides a weaker signal than the probe of the first region on reaction with the reference nucleic acid, and

the third region containing at least one probe which provides no signal on reaction with the reference nucleic acid.